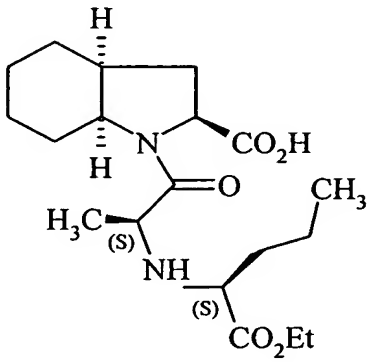
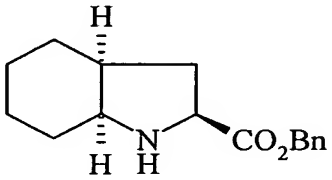
CLAIMS

1. Process for the industrial synthesis of perindopril of formula (I)

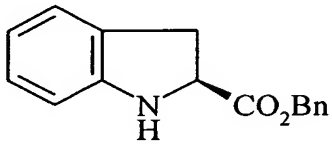


(I)

and pharmaceutically acceptable salts thereof, characterised in that the benzyl ester of formula (IIa) or (IIb) :



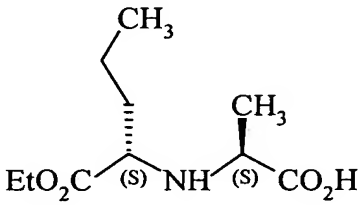
(IIa)



(IIb)

or an addition salt of the ester of formula (IIa) or (IIb) with a mineral acid or organic acid is reacted

with the compound of formula (III) :



(III)

in the presence of a coupling agent selected from the following reagents and pairs of reagents :

(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride,

(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 1-hydroxybenzotriazole,

(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 1-hydroxy-7-azabenzotriazole,
(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / N-hydroxysuccinimide,
(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazine,
(1,3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride / N-hydroxyphthalimide,
dicyclohexylcarbodiimide / 1-hydroxy-7-azabenzotriazole,
dicyclohexylcarbodiimide / N-hydroxysuccinimide,
dicyclohexylcarbodiimide / 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazine,
dicyclohexylcarbodiimide / N-hydroxyphthalimide,
O-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate,
O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate,
O-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate,
benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate,
benzotriazol-1-yl-oxy-tris(dimethylamino)phosphonium hexafluorophosphate,
O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate,
O-(benzotriazol-1-yl)-1,1,3,3-bis(pentamethylene)uronium hexafluorophosphate,
chloro-tripyrrolidinophosphonium hexafluorophosphate,
chloro-1,1,3,3-bis(tetramethylene)formamidinium hexafluorophosphate,
chloro-1,1,3,3-bis(pentamethylene)formamidinium hexafluorophosphate,
N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline,
O-[(ethoxycarbonyl)-cyanomethyleneamino]-1,1,3,3-tetramethyluronium tetrafluoroborate,
O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate,
O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate / 1-hydroxybenzotriazole,
O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate / N-methylmorpholine,
O-(3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate / collidine,
O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate,

O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate / 1-hydroxybenzotriazole,
O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate,
O-(1,2-dihydro-2-oxo-1-pyridyl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate / 1-hydroxy-benzotriazole,
O-(N-succinimidyl)-1,1,3,3-tetramethyluronium tetrafluoroborate,
O-(N-succinimidyl)-1,1,3,3-bis(tetramethylene)uronium tetrafluoroborate,
O-(N-succinimidyl)-1,1,3,3-bis(tetramethylene)uronium tetrafluoroborate / 1-hydroxy-benzotriazole,
O-(5-norbornene-2,3-dicarboximido)-1,1,3,3-tetramethyluronium tetrafluoroborate,
propanephosphonic anhydride,
N-hydroxy-5-norbornene-2,3-dicarboxylic acid imide,
and N-hydroxy-1,2-dihydro-2-oxo-pyridine,

optionally in the presence of a base,
to yield, after catalytic hydrogenation in the presence of palladium, perindopril of formula (I), which is converted, if desired, into a pharmaceutically acceptable salt.

2. Process according to claim 1 for the synthesis of perindopril in the form of its tert-butylamine salt.

3. Process according to claim 1, characterised in that the compound of formula (IIa) is used as starting material.

4. Process according to claim 1, characterised in that the compound of formula (IIb) is used as starting material.

5. Process according to claim 3, characterised in that the hydrogenation reaction is carried out under a hydrogen pressure of less than 10 bars.

6. Process according to claim 4, characterised in that the hydrogenation reaction is carried out under a hydrogen pressure of from 10 to 35 bars.